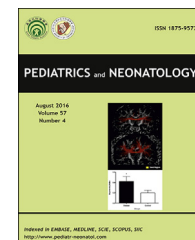


Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.pediatr-neonatal.com>

Letter to the Editor

Slow oral immunotherapy for cow's milk allergy with anaphylaxis to extensively hydrolyzed formula

Cow's milk (CM) is a common allergen present in immunoglobulin E (IgE)-mediated food allergy in children. The management of CM allergy (CMA) requires the replacement of milk protein with alternative protein and calcium sources. Extensively hydrolyzed formulas (eHFs) are alternative, hypoallergenic formulas that are recommended as standards for children with CMA.¹ IgE-mediated immediate reactions to eHFs, such as life-threatening anaphylaxis, rarely occur.² Patients with hyperresponsiveness to eHFs may be at a high risk because they are on a complete elimination diet.

Oral immunotherapy (OIT) is an intervention that is used for treating IgE-mediated food allergy. Regular consumption with increasing food allergen doses could induce desensitization. CM-OIT has shown effective results through in-hospital rush and home-based slow protocols.^{3,4} It remains unknown whether OIT could desensitize severely allergic patients with CMA with a history of anaphylaxis to eHFs. This is, to the best of our knowledge, the first report on a clinical possibility of OIT for such patients.

A five-year-old girl was admitted to our hospital for the treatment of food allergy. She presented with complications of bronchial asthma and atopic dermatitis. She was exclusively breastfed since birth. At the age of five months, the family doctor recommended that she should avoid CM because she had eczema and positive serum CM-specific IgE. After the complete avoidance of CM for three years, she tried some eHF at home for supplementing the calcium, which resulted in anaphylaxis. At the first visit to our hospital, serum CM-specific IgE was measured to be 37.1 UA/mL using ImmunoCAP assay (Phadia, Thermo Fisher Scientific, Uppsala, Sweden). She underwent oral food challenge (OFC) with casein-based eHF (new MA-1, Morinaga Co. Inc,

Osaka, Japan). After an intake of 20 mL of eHF, she developed anaphylaxis, presenting with skin rashes, sneezing, severe cough, and dyspnea. On the following day, OFC using 1 mL of eHF showed no symptoms and she commenced OIT through a home-based slow protocol. She consumed 1 mL of eHF at home every day and increased it by 20%–50% in the outpatient clinic of the hospital approximately every 2–4 weeks (Fig. 1). Vigorous exercise was avoided for 2 h following CM consumption. Furthermore, the patient was instructed to avoid eHF or CM when affected by infection, asthma attack, or any other unfavorable physical conditions. After reaching 50 mL of eHF, OFC with 24 mL of fermented CM drink, containing 12.3 mg/mL of CM protein, presented with urticaria and wheezing with hypoxemia. On the following day, an OFC with 0.5 mL of fermented CM drink showed no allergic reaction and OIT was continued. Fermented CM drink was used for 12 months because at first she did not want to drink CM directly. Upon the occurrence of adverse reactions, the daily dose was reduced to the extent determined by attending doctors. After 68 months, she achieved 200 mL of CM. She maintained the daily consumption for six months, and subsequently reduced the frequency to alternate days. During the up-dosing period, she developed anaphylaxis requiring intramuscular adrenaline injection once, and urticaria or mild respiratory symptoms occurred several times. After reaching the maintenance period, she occasionally showed very mild urticaria caused by CM consumption, which indicated that she had achieved desensitization, not natural resolution.

The course of the patient suggests two important clinical issues: First, patients with CMA can develop anaphylaxis to eHFs. Second, these patients can be treated with slow OIT. It can be concluded that the patient achieved

<https://doi.org/10.1016/j.pedneo.2019.12.007>

1875-9572/Copyright © 2020, Taiwan Pediatric Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Please cite this article as: Horino S et al., Slow oral immunotherapy for cow's milk allergy with anaphylaxis to extensively hydrolyzed formula, Pediatrics and Neonatology, <https://doi.org/10.1016/j.pedneo.2019.12.007>

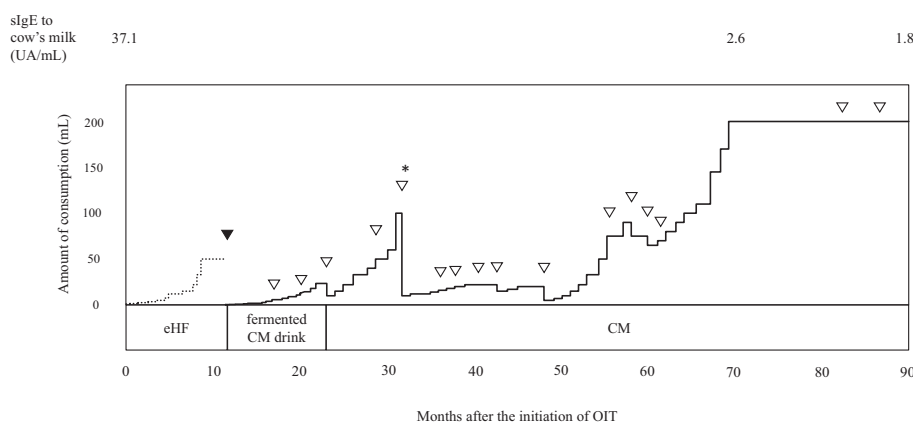


Figure 1 Clinical course of oral immunotherapy. Extensively hydrolyzed formula (dotted line) was consumed every day for the first 12 months, followed by the daily consumption of fermented CM drink or CM (solid line). The amount of fermented CM drink was presented as an equivalent amount of CM. The black triangle shows anaphylaxis requiring intramuscular adrenaline injection. The white triangles show immediate allergic symptoms not requiring adrenaline injection. *The dose of CM was reduced to 10 mL because the patient strongly wished to decrease the dose after severe urticaria. CM, cow's milk; eHF, extensively hydrolyzed formula; OIT, oral immunotherapy; sIgE, specific IgE.

desensitization to CM and the risk of life-threatening accidents was reduced following OIT.

controlled study. *Ann Allergy Asthma Immunol* 2010;105:376–81.

Declaration of Competing Interest

The authors declare no conflict of interests.

References

1. Fiocchi A, Brozek J, Schünemann H, Bahna SL, von Berg A, Beyer K, et al. World allergy organization (WAO) diagnosis and rationale for action against cow's milk allergy (DRACMA) guidelines. *Pediatr Allergy Immunol* 2010;21:1–125.
2. Antunes J, Borrego LM, Queiroz A, Chambel M, Rosa S, Romeira A, et al. Allergy to extensively hydrolysed formulas. *Allergol Immunopathol (Madr)* 2009;37:272–4.
3. Longo G, Barbi E, Berti I, Meneghetti R, Pittalis A, Ronfani L, et al. Specific oral tolerance induction in children with very severe cow's milk-induced reactions. *J Allergy Clin Immunol* 2008;121:343–7.
4. Pajno GB, Caminiti L, Ruggeri P, De Luca R, Vita D, La Rosa M, et al. Oral immunotherapy for cow's milk allergy with a weekly up-dosing regimen: a randomized single-blind

Satoshi Horino*
Department of Allergy, Miyagi Children's Hospital, Sendai,
Japan

Taiki Satou
Department of Allergy, Miyagi Children's Hospital, Sendai,
Japan
Department of Pediatrics, Japanese Red Cross Sendai
Hospital, Sendai, Japan

Masato Nihei
Katsushi Miura
Department of Allergy, Miyagi Children's Hospital, Sendai,
Japan

*Corresponding author. Department of Allergy, Miyagi Children's Hospital, 4-3-17 Ochiai, Aoba-ku, Sendai, 989-3126, Japan. Fax: +81 022 391 5118.

E-mail addresses: horino-thk@umin.ac.jp, horino-s@miyagi-children.or.jp (S. Horino)